Specific pathogens and problems: *Pseudomonas aeruginosa*

Lancet Conference on Managing Healthcare-associated Infections

London, December 2008

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P. aeruginosa – a formidable adversary

Respiratory tract

- Pneumonia
  - Hospital-acquired pneumonia
    - Ventilator-associated pneumonia
- Exacerbation of chronic lung condition
  - Bronchiectasis
  - Cystic Fibrosis

Blood

- Bacteraemia/Septicaemia
  - Neutropenia
  - Device-related

Urinary tract

- Acute/Chronic
  - Catheter related
  - Urinary tract surgery

Skin and soft tissue

- Burn wound sepsis
- Wound infection
- Ecthyma gangrenosum
- Folliculitis
- "Diabetic foot"

Eye

- Endophthalmitis
  - Post-surgical
- Keratitis

Ear

- Malignant otitis externa

Bone and joint

- Osteomyelitis
- Septic arthritis

P. aeruginosa – a formidable adversary

- National Healthcare Safety Network (subsumes NNIS)
- 463 US Hospitals from Jan 06 – Oct 2007
- 28 502 HCAI in 25 384 patients

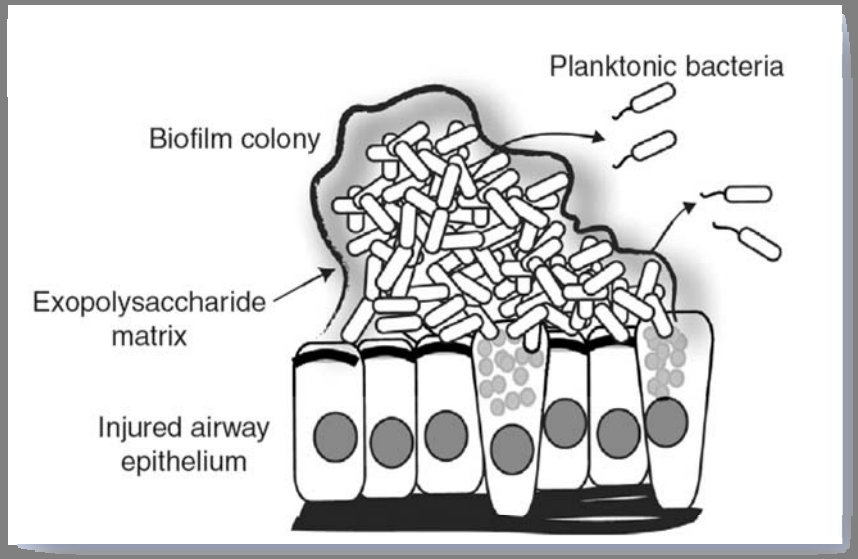
- *P aeruginosa* (rank order)
  - Overall: 6th
  - CRBSI: 7th
  - CAUTI: 4th
  - VAP: 2nd
  - SSI: 5th

Hidron *et al Infect Control Hosp Epidemiol* 2008:29:996-1011

P. aeruginosa – a formidable adversary

Virulence factors

- Proteases
- Elastase
- Rhamnolipids
- Phenazines
  - pyocyanin
- Type III secretion system
  - Exo S, Exo T, Exo U, Exo Y
- Type IV pili
- Biofilm formation



Driscoll *et al Drugs* 2007:67;351-368

P. aeruginosa – a formidable adversary

Mechanism	Resistance conferred
Multidrug efflux pumps e.g. MexA-MexB-OprM MexC-MexD-OprJ MexE-MexF-OprN MexX-MexY-OprM	Cephalosporins Fluoroquinolones Ureidopenicillins Carbapenems Aminoglycosides
β-lactamases AmpC ESBLs (e.g. VEB, GES, OXA, PER, BEL) Metallo-β-lactamases (IMP, VIM, SPM, GIM, SIM, AIM)	Penicillins, Cephalosporins Carbapenems
Aminoglycoside-modifying enzymes [e.g. AAC(3)-I, AAC(6')-II	Aminoglycosides
Outer membrane permeability loss OprD porin	Carbapenems
Target modification e.g. gyrA, parC	Fluroquinolones

TABLE 2

Proportion of non-susceptible *Pseudomonas aeruginosa* strains isolated in 33 European countries participating in the European Antimicrobial Resistance Surveillance System (EARSS) in 2007

Country	Proportion (%) of strains non-susceptible to:				
	Aminoglycosides[a]	Carbapenems[b]	Quinolones[c]	Ceftazidime	Piperacillins[d]
Austria	11.2	13.7	17.9	9	7.1
Switzerland	4.8	5.4	7.2	4.2	5
Cyprus	25	21.1	21.2	15.4	28.8
Czech Republic	33.8	36	42.7	32.7	30
Germany	20.3	31.5	35.7	24.4	48.5
Denmark	2.4	3.9	9.1	4	4.8
Spain	23.9	18.4	27.7	15.2	8.1
Finland	8.7	9.4	10.9	7.7	7.3
France	31.1	18.4	26.3	18.6	20.5
Greece	51.9	50.5	51.9	44.8	38.4
Croatia	43.4	28.1	33	20.5	30.2
Hungary	34.4	21.3	29.5	15.3	16.8
Ireland	12.5	11.2	20.5	10.3	11.8
Israel	21.9	14.9	26.7	13.3	15.2
Italy	30.1	32.1	39.1	41.4	27.2
The Netherlands	9.8	5.4	9.4	5.6	5.2
Norway	1.9	14.5	10.7	6.7	3.1
Poland	40.3	22.4	40.3	22.7	35.8
Portugal	18.2	16.1	23	20.9	15.8
Sweden	0	9	10.3	9.6	3.1
Slovenia	13.6	20.4	18.1	13.6	12.5
Turkey	28.2	31	29.6	31.3	32.4
United Kingdom	6.6	17.2	9.6	14.1	5.4

Souli *et al Eurosurveillance* 2008 13 (47):1 - 11

Resistance in *P. aeruginosa* isolates from the ICU

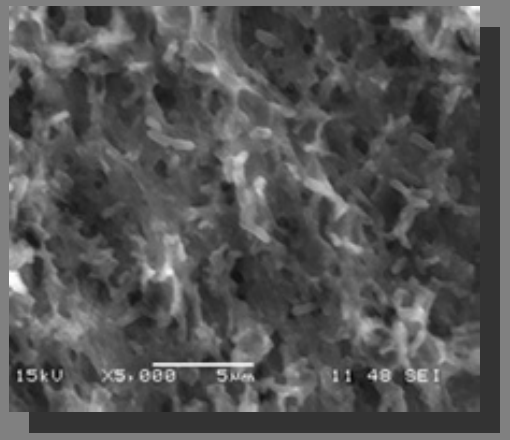
	Croatia	Czech Rep	Estonia	Hungary	Malta	Romania	Sweden	Turkey
No of ICUs	4	3	3	8	3	1	10	3
Ceftazidime	11.0	34.4	5.5	10.7	9.7	34.0	11.0	48.3
Ciprofloxacin	36.2	28.9	5.0	20.5	23.8	55.3	12.2	37.8
Imipenem	28.3	30.3	13.7	18.8	25.4	10.6	17.3	48.4
Aminoglycoside	42.3	26.2	4.7	22.7	9.3	57.4	0.0	53.5

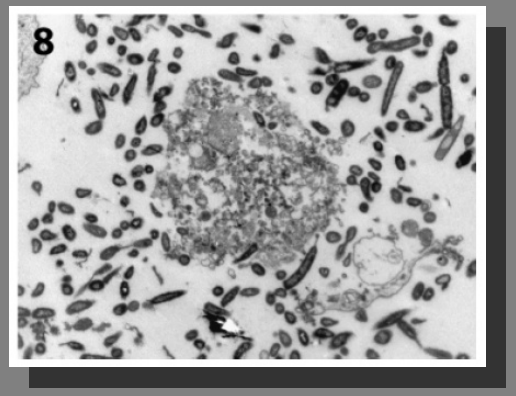
Infection Control Intervention	Number (%)
Isolation of patients infected/colonised with multi-resistant P. aeruginosa	6/14 (43)
Antibiotic guidelines for management of ICU-acquired infections	10/20 (50)

Hanberger *et al Intensive Care Med* In press

P. aeruginosa – a formidable adversary

- Environmental persistence
  - Potable water
  - Taps/sinks/sink traps
  - Showers
  - Disinfectants/sanitisers
  - Respiratory therapy equipment
  - Ice-makers
  - Flower vases
  - Shaving/toothbrushes
  - Hydrotherapy pools
  - Mop heads/buckets
  - Bronchoscopes
  - Contact lens cleaning materials
  - Hand lotions
  - Multi-dose vials
  - Bath toys





Matz *et al ISME Journal* (2008) **2,** 843–852

P. aeruginosa infection: prevention is better than cure

- Antimicrobial stewardship
- Conventional infection control
- Elimination of environmental reservoirs

Antimicrobial stewardship and *P. aeruginosa*

Intervention	Duration	Desired Outcome	Undesired Outcome
Ciprofloxacin + ceftazidime[1]	18 months	CIP R ↓ CAZ R ↓	MEM R↑
Ciprofloxacin[2]	34 months	CIP R ↓	MEM R↑

[1] Ntagiopoulos *et al Int J Antimicrob Ag* 2007:30;360–365
[2] Cook *et al Infect Control Hosp Epidem* 2008:29;716-722

Antimicrobial stewardship and *P. aeruginosa*

- 35 ICUs from 1999-2004

TABLE 2. Genodiversity of Imipenem- or Ciprofloxacin-Resistant Isolates Among Different Groups of Intensive Care Units (ICUs), Stratified by Relative Resistance Rate (RR) and Antimicrobial Usage Diversity (AUD)

ICU class, ICU group	No. of ICUs	No. of resistant isolates / no. tested for antimicrobial susceptibility	No. of typed isolates	No. of ICU-based genotypes	ICU-group diversity[a]	Significant difference in diversity, compared with ICU group(s)[b]
Ciprofloxacin-resistant isolates recovered[c]						
A (>median RR, ⩽median AUD)	8	229/841	123	66	0.50	D
B (>median RR, >median AUD)	7	196/666	40	25	0.54	D
C (⩽median RR, ⩽median AUD)	7	109/942	61	42	0.64	D
D (⩽median RR, >median AUD)	8	58/892	49	45	0.90	A, B, C
Imipenem-resistant isolates recovered[d]						
A (>median RR, ⩽median AUD)	4	136/415	72	38	0.50	B, C, D
B (>median RR, >median AUD)	10	447/1,231	140	103	0.71	A, D
C (⩽median RR, ⩽median AUD)	11	88/1,006	79	60	0.72	A, D
D (⩽median RR, >median AUD)	4	55/372	26	25	0.95	A, B, C

Jonas *et al* *Infect Control Hosp Epidem* 2008:28;350-7

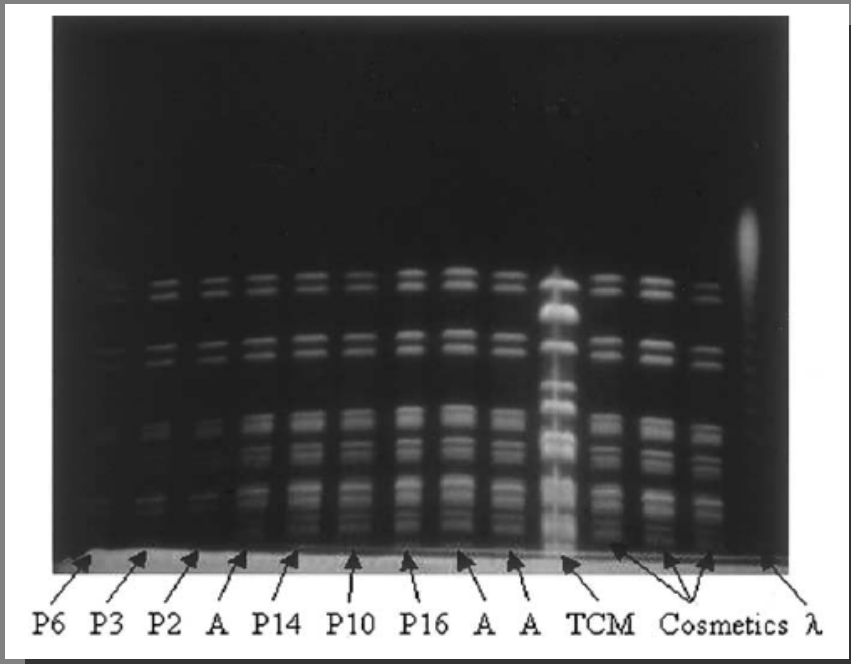
Control of *P. aeruginosa*: back to basics

TABLE 3
MULTIVARIATE ANALYSIS OF RISK FACTORS FOR ACQUIRING *PSEUDOMONAS AERUGINOSA* WITHIN THE FIRST 2 WEEKS OF HOSPITALIZATION IN A NEONATAL INTENSIVE CARE UNIT, OKLAHOMA CITY, MARCH 1, 1997, THROUGH MARCH 22, 1998

Characteristics	OR* (CI_{95})	*P*
Exposure to nurse A1	10.37 (2.86-37.58)	<.001
Exposure to nurse B	3.08 (1.02-9.32)	<.05

Abbreviations: CI_{95}, 95% confidence interval; OR, odds ratio.
* ORs were adjusted for birth-weight category.

Moolenaar *et al Infect Control Hosp Epidem* 2000:21;80-5



McNeil *et al Clin Infect Dis* 2001:33;317-23

P. aeruginosa and the hospital environment: cause for concern or case for complacency?

P. aeruginosa and hospital water: prospective studies

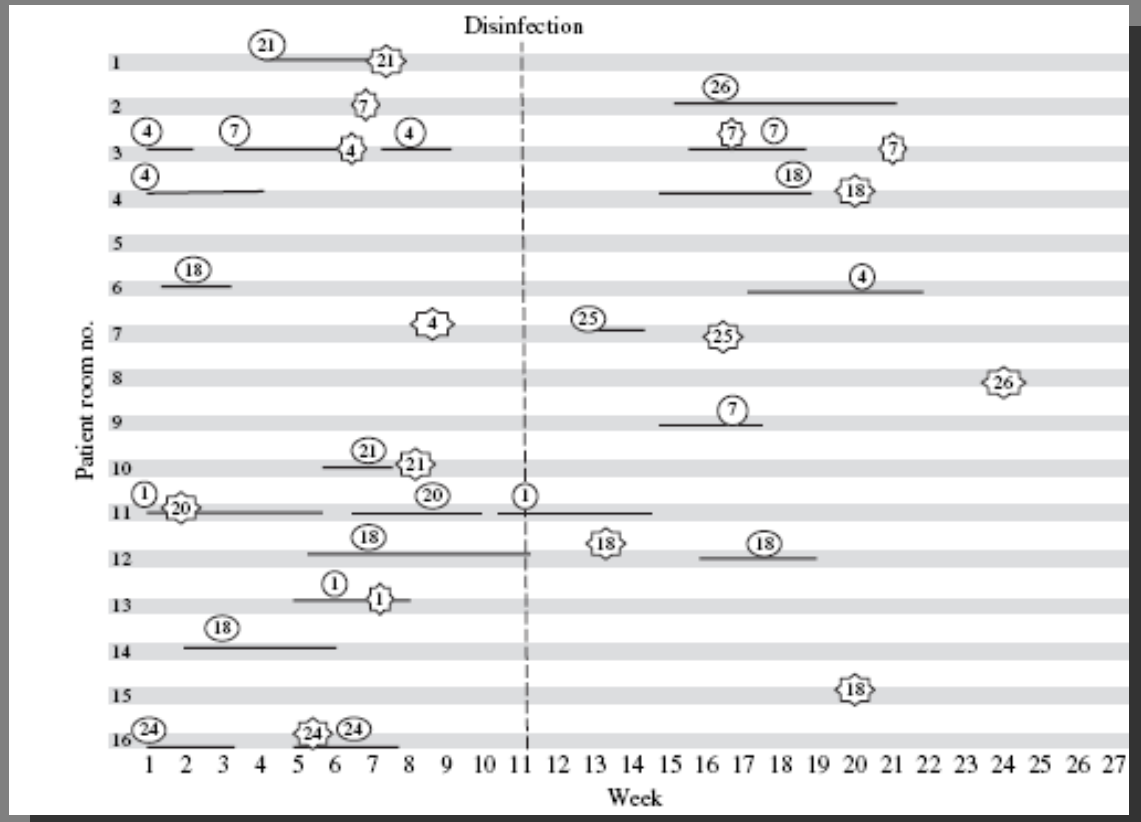
- Frequency of patient/water sampling
- Site of patient sampling (single *v* multiple)
- Environmental sampling: water +/- taps
- Sampling methods (volume/culture media/etc)
- Numbers of colonies selected for molecular typing

P. aeruginosa and hospital water – prospective studies

- 16-bed medical ICU over 6 month period
- Weekly tap water samples obtained (n=57)
- *P. aeruginosa* from 11.4% of samples from patients' rooms *cf* 5.3% samples from other areas
- Patients sampled on admission and weekly thereafter
- *P. aeruginosa* from 32 patients
- Isolates typed by *Spe1* PFGE

Rogues *et al J Hosp Infect* 2007:67;72-78

P. aeruginosa and hospital water – prospective studies



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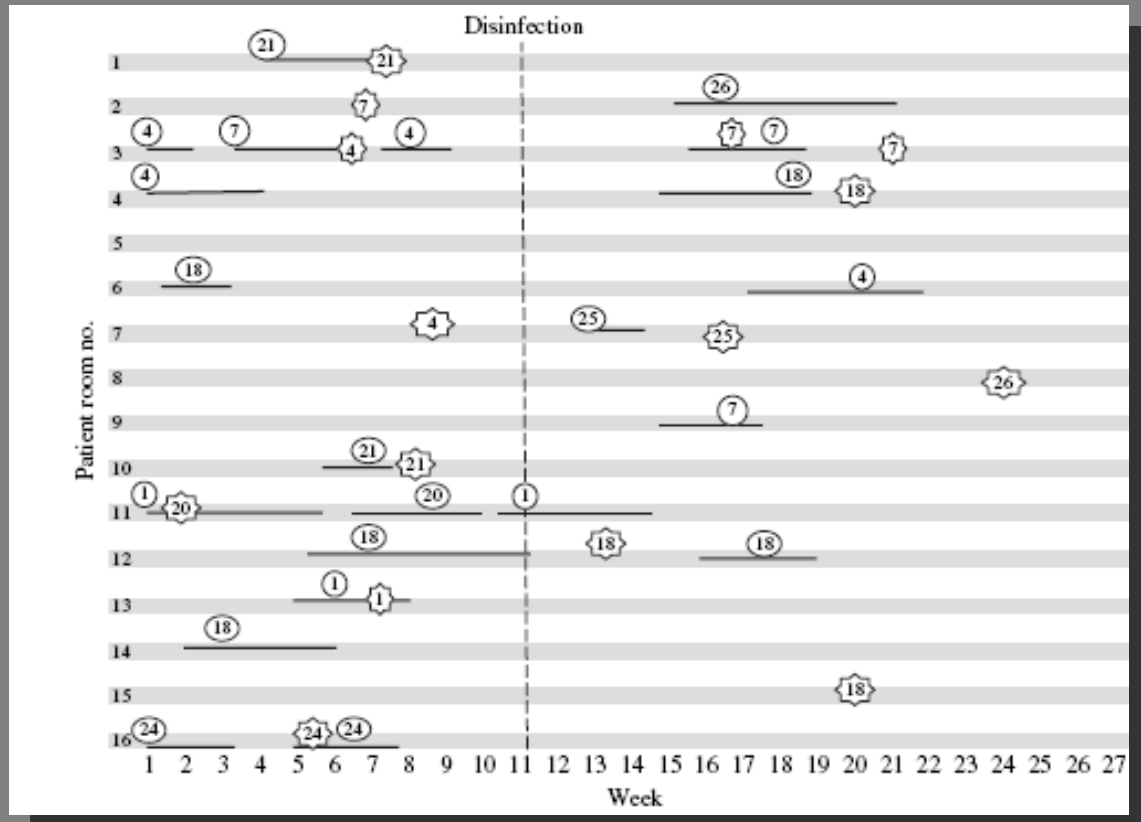
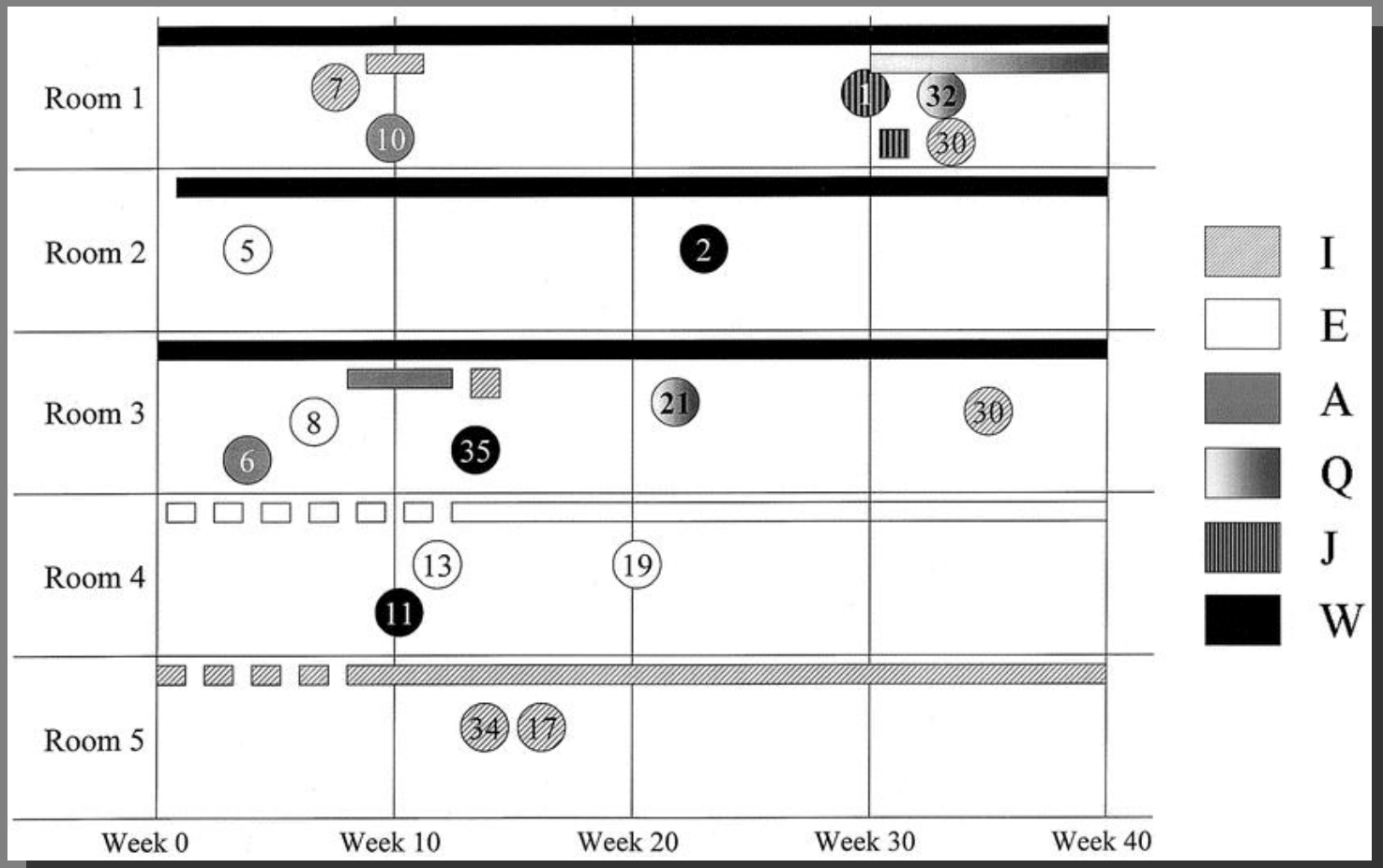
P. aeruginosa and hospital water – prospective studies



Rogues *et al J Hosp Infect* 2007:67;72-78

Strategies for elimination of *P. aeruginosa* from hospital water



Intensive programme of cleaning and autoclaving of aerators unsuccessful

Trautmann *et al Infect Control Hosp Epidemiol* 2001: 22; 49-52

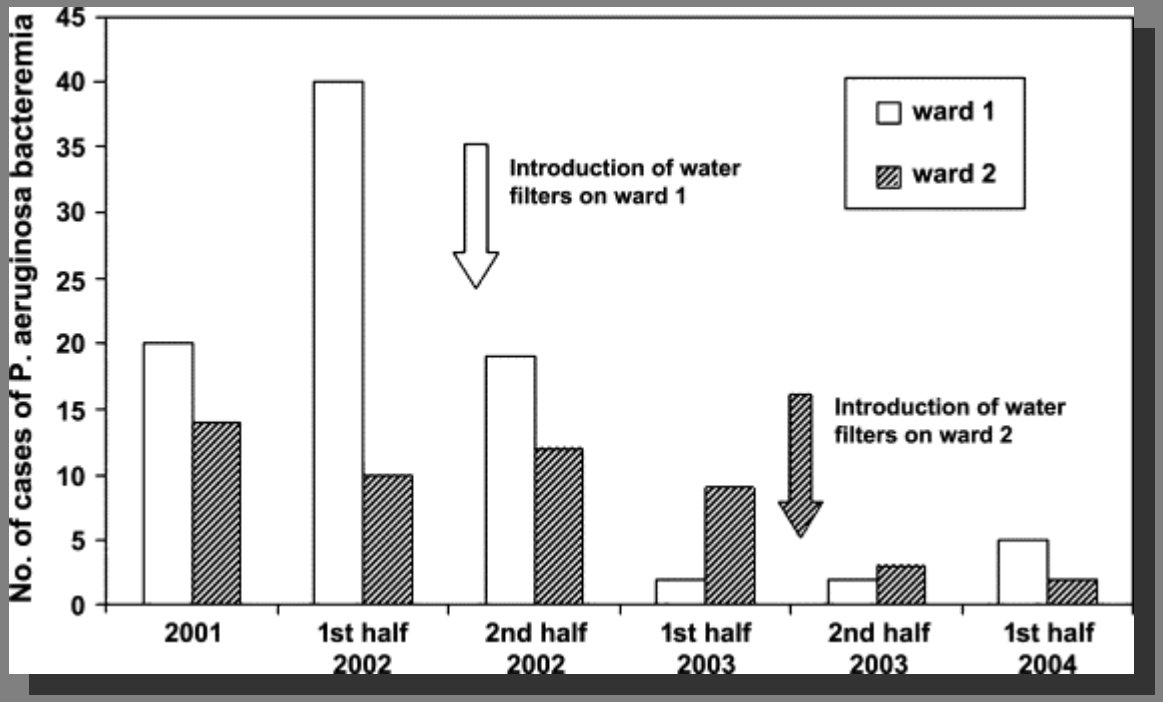
Reuter *et al Crit Care Med* 2002:30;2222-2228

Approaches to eradication of bacteria from hospital water

Method	Ease of deployment	Cost	Maintenance	Disadvantages
Heat	Easy	Low	Easy	Need to maintain consistent temperature Recolonisation at low temperatures May be hard to disinfect dead leg pipes Scalding potential May result in increase in biofilm sloughing Labour intensive
Chlorine	Difficult	High	Fair/difficult	Amoebae are resistant to chlorine Recolonisation after disinfection Corrosion of pipework (leading to increased biofilm formation) Need to check chlorine levels Does not penetrate established biofilms Production of trihalomethanes
Chlorine dioxide	Fair	Low/moderate	Fair/difficult	Does not penetrates established biofilms ? corrosive properties
Monochloramines	Fair	Moderate	Fair/difficult	? ability to penetrate biofilms Must remove if water to be used for dialysis
Cu^{++}/Ag^{++} ionisation	Fair	Low/moderate	Moderate	Water must have low content of dissolved solids Can corrode some types of pipework Scale problems
UV	Fair	Moderate	Requires cleaning to allow effective activity	Penetrates established biofilms poorly
Ozone	Difficult	High	Moderate	Disinfects only at the point of injection Decomposes quickly in hot water Need to maintain set concentration for efficacy

Adapted from Ortolano *et al Am J Infect Control* 2004;33 (suppl 1): S1-14

Point of use filtration – does it work in “real life” settings?



Vianelli *et al Haematologica* 2006:91;983-5

Point-of-use filters in the ICU: a prospective study

- 11-bedded surgical ICU (3 x 1; 4 x 2)
- *P. aeruginosa* colonisation/infection in year before introduction of filters compared with 12-month period after all patient-related outlets fitted with filters
- Water outlets sampled at two weekly intervals in 6 months before introduction of filters
- Patient and water isolates typed using RAPD-PCR

Trautman *et al Amer J Infect Control* 2008 36:421-429

Point-of-use filters in the ICU: a prospective study

- Water sampling

  Pre-filter: 113/117 (97%) grew *P. aeruginosa*

  109/113 (96%) > 10^2 cfu/mL

  Mains water: no growth

  Post-filter: 0/52

Trautman *et al Amer J Infect Control* 2008 36:421-429

Point-of-use filters in the ICU: a prospective study

- Genotyping
  - 113/113 (100%) water isolates clonotype A
  - 25/27 (92.6%) patient isolates clonotype A

Trautman *et al Amer J Infect Control* 2008 36:421-429

Variable	Pre-filter period	Post-filter period	P value
Total no. of admitted patients	649	585	
Mean duration of ICU stay (days ± 1 SD)	5.9 ± 9.4	5.8 ± 8.8	
No. of patients staying ≥3 days	304	282	
Mean duration of ICU stay in patients staying ≥3 days (days ± 1 SD)	10.5 ± 12.3	10.0 ± 11.3	
No. of *P. aeruginosa*-positive patients in patient group staying ≥3 days (%)	47 (15.5)	12 (4.3)	<.0001
No. of *P. aeruginosa*-positive patients in patient group staying ≥3 days fulfilling CDC criteria for infection (%)	34 (11.2)	10 (3.6)	.0003

Trautman *et al Amer J Infect Control* 2008 36:421-429

Point-of-use filters in the ICU: a prospective study

- Reduction in ceftazidime use ($P < 0.0001$)
- Reduction in carbapenem use (P 0.0015)
- Overall net savings of $64 000 (assuming twice weekly filter changes)

Trautman *et al Amer J Infect Control* 2008 36:421-429

Four conclusions...and a question

- There is increasing anti-microbial resistance in HCAI-associated strains of *Pseudomonas aeruginosa*…
- Antimicrobial stewardship programmes in hospital settings, especially in the ICU, are thus needed, although these cannot be regarded as the sole intervention to address this problem.
- The role of environmental reservoirs, especially hospital water supplies in the epidemiology of *Pseudomonas aeruginosa* on the ICU should not be underestimated…
- …and should be taken into account in developing infection control interventions especially in units where *P. aeruginosa* infections are endemic
- Should we accept that *P. aeruginosa* is just an inherent "occupational hazard" for vulnerable patients in hospital in non-outbreak situations?